

AMENDMENTS TO THE CLAIMS

Prior to prosecution on the merits, please enter the following amendments:

Please cancel, without prejudice, claims 4, 7-10, 14-22, 27-28, and 31-32.

Please add new claims 42-56.

1. **(Currently amended)** A method for promoting one or more of ~~modulating~~ growth, differentiation, or survival of a neuronal cell, comprising contacting said cell with an ~~effective~~ amount of a Sonic hedgehog polypeptide effective to promote one or more of growth, differentiation, or survival of said neuronal cell, wherein said Sonic hedgehog polypeptide binds a naturally occurring patched receptor.
2. **(Currently amended)** A method for promoting ~~modulating~~ one or more of growth, differentiation, or survival of a mammalian neuronal cell responsive to hedgehog induction, comprising contacting ~~treating~~ the cell with an ~~effective~~ amount of a Sonic hedgehog polypeptide effective to promote thereby altering, relative to the cell in the absence of hedgehog treatment, at least one of (i) rate of growth, (ii) differentiation, or (iii) survival of the cell, wherein said Sonic hedgehog polypeptide binds a naturally occurring patched receptor.
3. **(Original)** The method of claim 2, which polypeptide mimics the effects of a naturally-occurring hedgehog protein on said cell.
4. **(Cancelled)**
5. **(Currently amended)** The method of claim 2, wherein the ~~which~~ polypeptide comprises an amino acid sequence at least 90% identical or homologous to an amino acid sequence designated in at least one of SEQ ID No:8, SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, or an N-terminal fragment thereof of at least 100 contiguous amino acids that binds a naturally occurring patched receptor ~~or SEQ ID No:14.~~

6. **(Currently amended)** The method of claim 5, which polypeptide is an N-terminal auto-proteolytic ~~a bioactive~~ fragment of a hedgehog polypeptide.

7-10. **(Cancelled)**

11. **(Currently amended)** The method of claim 2, wherein the polypeptide promotes ~~modulates~~ the differentiation of said neuronal cell ~~cells~~.

12. **(Currently amended)** The method of claim 11, ~~which wherein said neuronal cell is cells are~~ selected from any the group consisting of a motor neuron neurons, a cholinergic neuron neurons, a dopaminergic dopanergic neuron neurons, a serotenergic neuron neurons, or and a peptidergic neuron neurons.

13. **(Currently amended)** The method of claim 11, wherein the polypeptide promotes survival of the said neuronal cell ~~cells~~.

14-22. **(Cancelled)**

23. **(Currently amended)** A method for inducing a cell to differentiate to a neuronal cell type phenotype, comprising contacting said cell with an amount of a Sonic hedgehog polypeptide effective to induce said cell to differentiate to a neuronal cell type, wherein said Sonic hedgehog polypeptide binds a naturally occurring patched receptor.

24. **(Currently amended)** The method of claim 23, wherein said polypeptide comprises an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a nucleic acid sequence selected from any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said polypeptide binds a naturally occurring patched receptor ~~which polypeptide comprises an amino acid sequence identical or homologous to amino acid sequence designated in one of SEQ ID No:8, SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No. 34, SEQ ID No.~~

~~40, SEQ ID No. 41, or homologs thereof.~~

25. **(Currently amended)** The method of claim 24, which polypeptide is a bioactive fragment of a Sonic hedgehog polypeptide, and wherein said bioactive fragment binds a naturally occurring patched receptor.

26. **(Currently amended)** The method of claim 23, wherein said neuronal cell ~~type~~ phenotype is selected from ~~any the group consisting of~~ motor neurons, cholinergic neurons, dopaminergic ~~dopaminergic~~ neurons, serotonergic neurons, and peptidergic neurons.

27-28. **(Cancelled)**

29. **(Currently amended)** A method for treating a degenerative disorder of the nervous system characterized by neuronal cell death, comprising administering to a patient a therapeutically effective amount of a pharmaceutical preparation of a Sonic hedgehog polypeptide thereby causing, relative to the absence of hedgehog treatment, prolonged survival of neural cells in said patient, wherein said Sonic hedgehog polypeptide binds a naturally occurring patched receptor.

30. **(Currently amended)** The method of ~~claim~~ claim 29, wherein said Sonic hedgehog polypeptide comprises an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a nucleic acid sequence selected from any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said polypeptide binds a naturally occurring patched receptor identical or homologous to a polypeptide selected from the group consisting of SEQ ID No:8, SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, and SEQ ID No:14, or is a bioactive fragment thereof.

31-32. **(Cancelled)**

33. **(Original)** The method of claim 29, wherein said therapeutically effective amount of hedgehog polypeptide inhibits the de-differentiation of neural cells of said patient.

34. **(Original)** The method of claim 33, wherein said neural cell is a glial cell.
35. **(Original)** The method of claim 33, wherein said neural cell is a nerve cell.
36. **(Original)** The method of claim 29, wherein said degenerative disorder is a neuromuscular disorder.
37. **(Original)** The method of claim 29, wherein said degenerative disorder is a autonomic disorder.
38. **(Original)** The method of claim 29, wherein said degenerative disorder is a central nervous system disorder.
39. **(Currently amended)** The method of claim 29, wherein said degenerative disorder is selected from any a group consisting of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Pick's disease, Huntington's disease, multiple sclerosis, neuronal damage resulting from anoxia-ischemia, neuronal damage resulting from trauma, or and neuronal degeneration associated with a natural aging process.
40. **(Original)** The method of claim 29, further comprising administering to said patient a therapeutically effective amount of a growth factor having neurotrophic activity.
41. **(Currently amended)** The method of claim 40, wherein said growth factor is selected from any a group consisting of a nerve growth factor, ciliary neurotrophic growth factor, schwannoma-derived growth factor, glial growth factor, striatal-derived neuronotrophic factor, or platelet-derived growth factor.
42. **(New)** The method of claim 1, wherein said hedgehog polypeptide comprises an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step

of 0.2X SSC at 65 °C, to a nucleic acid sequence selected from SEQ ID No: 1, SEQ ID No: 4, SEQ ID No: 5, and SEQ ID No: 6, and wherein said hedgehog polypeptide binds to a naturally occurring patched receptor.

43. (New) The method of claim 2, wherein said hedgehog polypeptide comprises an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a nucleic acid sequence selected from SEQ ID No: 1, SEQ ID No: 4, SEQ ID No: 5, and SEQ ID No: 6, and wherein said hedgehog polypeptide binds to a naturally occurring patched receptor.

44. (New) The method of claim 42, wherein said hedgehog polypeptide comprises an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, and wherein said hedgehog polypeptide binds a naturally occurring patched receptor.

45. (New) The method of claim 43, wherein said hedgehog polypeptide comprises an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, and wherein said hedgehog polypeptide binds a naturally occurring patched receptor.

46. (New) The method of claim 6, wherein said hedgehog polypeptide comprises an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, and wherein said hedgehog polypeptide binds a naturally occurring patched receptor.

47. (New) The method of claim 42, wherein said hedgehog polypeptide comprises an amino acid sequence designated in one of SEQ ID No: 8, SEQ ID NO: 11, SEQ ID No: 12, SEQ ID No: 13, or an N-terminal fragment of at least 100 contiguous amino acids thereof that binds to a naturally occurring *patched* receptor.

48. (New) The method of claim 43, wherein said hedgehog polypeptide comprises an amino acid sequence designated in one of SEQ ID No: 8, SEQ ID NO: 11, SEQ ID No: 12, SEQ ID No: 13, or an N-terminal fragment of at least 100 contiguous amino acids thereof that binds to a naturally occurring *patched* receptor.

49. (New) A method for inducing a cell to differentiate to a neuronal cell phenotype, comprising contacting said cell with an amount of a Sonic hedgehog polypeptide comprising an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a nucleic acid sequence selected from SEQ ID No: 1, SEQ ID No: 4, SEQ ID No: 5, and SEQ ID No: 6, wherein said hedgehog polypeptide binds to a naturally occurring patched receptor, and wherein said amount is effective to induce a cell to differentiate to a neuronal cell phenotype.

50. (New) The method of claim 49, wherein said hedgehog polypeptide comprises an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, and wherein said hedgehog polypeptide binds a naturally occurring patched receptor.

51. (New) The method of claim 49, wherein said neuronal cell phenotype is selected from motor neurons, cholinergic neurons, dopaminergic neurons, serotonergic neurons, and peptidergic neurons.

52. (New) A method for promoting one or more of growth, differentiation, or survival of a neural stem cell, comprising contacting the cell with an amount of a Sonic hedgehog polypeptide comprising an amino acid sequence encoded by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C or higher stringency, to a nucleic acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, wherein said hedgehog polypeptide binds to a naturally occurring patched receptor, and wherein said amount is effective to promote growth, differentiation, or survival of the neural stem cell.

53. (New) The method of claim 52, wherein said polypeptide comprises an N-terminal auto-proteolytic fragment of a hedgehog polypeptide, and polypeptide binds a naturally occurring patched receptor.

54. (New) The method of claim 52, wherein said hedgehog polypeptide promotes differentiation of said neural stem cell.

55. (New) The method of claim 54, wherein said hedgehog polypeptide promotes differentiation of said neural stem cell to a glial cell.

56. (New) The method of claim 54, wherein said hedgehog polypeptide promotes differentiation of said neural stem cell to a neuron.